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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
QIAN, CELINE X	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 11/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/830,703	LUBBERT, HERMANN	
	Examiner	Art Unit	
	Celine X Qian	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 August 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-8,13-15,17,18,20,22-28,30-34 and 36-38* is/are pending in the application.

4a) Of the above claim(s) *1,3-7,13,17,18,20,23-28 and 30-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8,14,15,22,33,34 and 36-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 April 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1, 3-8, 13-15, 17, 18, 20, 22-28, 30-34, 36-38 are pending in the application. Claims 1, 3-7, 13, 17, 18, 20, 23-28 and 30-32 are withdrawn from consideration for being directed to non-elected subject matter. Claims 8, 14, 15, 22, 33, 34, 36-38 are currently under examination.

This Office Action is in response to the Amendment filed on 8/20/03.

Response to Amendment

The objection to the specification has been withdrawn in light of Applicants' submission of an abstract.

The rejection of claims 14 and 22 under 35 U.S.C. 101 has been withdrawn in light of Applicants' amendment of the claims.

The rejection of claims 8, 15, 22 and 29 under 35 U.S.C. 112 2nd paragraph has been withdrawn in light of Applicants' amendment of the claims.

The rejection of claim 22 under 35 U.S.C. 102 (b) has been withdrawn in light of Applicants' amendment of the claim.

Claims 8, 14, 15, 22 and newly added claims 33, 34, 36-38 stand rejected under 35 U.S.C. 112 1st paragraph (written description and enablement) for reasons set forth of the record mailed on 1/28/03 and further discussed below.

The rejection of claim 14 under 35 U.S.C. 112 2nd paragraph is maintained for reasons set forth of the record mailed on 1/28/03 and further discussed below.

Response to Arguments

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8, 14, 15, 22, 33, 34, 36-38 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In response to this rejection, Applicants argue that the teaching of the specification is sufficient for making a transgenic animal comprising a polynucleotide encoding a mutant parkin2 which causes Parkinson's symptoms in human. Applicants assert that the list of mutant parkin2 that cause Parkinson's symptoms in human is taught in the specification. Applicants further assert that the mouse parkin2 share high sequence homology with the human counterpart. Applicants thus conclude that mutation at the same position in mouse gene would produce same Parkinson's symptoms as those seen in human. Applicants also assert that the specification has taught specific mutations with respect to a specific phenotype in human, thus the specification is enabling for a transgenic mouse or rat that has the same mutation would produce the same phenotype(s) that is seen in human. Applicants further point out that the Wall reference is outdated and does not teach Applicants' invention, in which a clear structural-functional relationship among the parkin2 gene mutations (human and mouse) and phenotype (human)

is known. Finally, Applicants cite Mullin et al., 1990, Breban et al., 1998, Hooper et al., 1992, Capecchi et al., 1994 and DePamphilis 1988, and conclude that these references support the generation of transgenic mouse and rat because they share sufficient similarities and embryonic stem cell availability.

These arguments have been fully considered but deemed unpersuasive. The detailed reasons for non-enablement of the claimed invention were discussed in detail in the office action mailed on 1/28/03. Based on the teaching of the prior art, the production of transgenic mouse or rat with a specific phenotype is unpredictable because of essential genetic control elements and genetic background varies from species to species (see page 5 of the previous office action). Although the human parkin2 share a high percentage of sequence similarity with the mouse homologue, whether the mouse parkin2 comprising the same mutation as the human would produce the same Parkinson symptoms is unpredictable because the genetic control elements and genetic backgrounds of human and rodent are very different. Although Applicants regard the Wall reference is outdated, Applicants fail to provide any more recent references that teach the phenotype of one transgenic specie is predictable of the same phenotype of another specie, in the instant case, from human to mouse. None of the references cited by Applicants teach such information (Applicants are invited to point out specific paragraph that provides such information). Contrary to Applicants' assertion, these references also fails to teach that embryonic stem cells of rat has been characterized. Although Breban et al. and Mullin et al. teach the generation of a transgenic rat, such method does not involve the use of rat embryonic stem cells. The method for making the specific mutation at a specific loci in a rat or mouse genome taught by the instant specification cannot be achieved without using embryonic stem

cells (see from line 10 of page 9 to line 31 of page 10). Therefore, the specification is not enabling for making a transgenic rat comprising said mouse parkin2 mutation. The specification is not enabling for making a transgenic mouse or rat comprising mouse parkin2 mutation that would have same phenotype as those seen in human Parkinson's disease patients. As such, the instant specification fails to teach how to make and use the claimed invention without undue experimentation. Consequently, this rejection is maintained.

Claims 8, 14, 15, 22, 33, 34, 36-38 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In response to the rejection, Applicants argue that the structural and functional relationship between a transgenic mouse harboring a mutation in parkin2 gene and the phenotype of said mouse is known because such relationship is known in human. Applicants argue the specification has listed a number of mutations in human parkin2 that are associated with Parkinson's symptom in human. Applicants thus conclude that the inventors had possession the invention at the time the application was filed.

The above arguments have been fully considered but deemed unpersuasive. As indicated in the previous office action, the homologue of the mouse mutant parkin2 gene encompasses potentially a large number of proteins that share certain homology with the mouse parkin2 gene. Without definition from the specification (a functional homologue or a structural homologue, for example), such genus of nucleotides may encompass sequences that encoding different protein.

Although the specification lists a number of mutations present in human parkin2, it is hardly representative of all the homologues of the claimed genus. In addition, even the structural-functional relationship between the human parkin2 and the phenotype is known. It does not extend to other homologues of different species or mutations at other sites within the parkin2 gene. As such, the specification fails to describe a representative number of species by their complete structure or other identifying characteristics. Therefore, the written description rejection is maintained.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 14 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 14 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: how to produce a transgenic mouse or rat from the chimeric mouse or rat.

In response to this rejection, Applicants argue that the production of a transgenic animal after the introduction of a blastocyst into a pseudopregnant female is known and within the skill of a person of ordinary skill in the art.

This argument has been considered but deemed unpersuasive. Applicants are reminded that a method claim always has to refer back to the preamble, in this case, a method of producing

a transgenic mouse or rat. However, the last step of claim 14 is obtaining a chimeric mouse or rat. Although an ordinary artisan may know how to produce a transgenic mouse or rat from that step, the claim itself has to be complete by reciting such step(s). Therefore, the rejection is maintained.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

This application contains claims 1, 3-7, 13, 17, 18, 20, 23-28 and 30-32 drawn to an invention nonelected with traverse in the amendment filed on 11/6/02. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X Qian whose telephone number is 703-306-0283. The examiner can normally be reached on 9:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 703-305-1998. The fax phone number for the organization where this application or proceeding is assigned is 703-305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Celine Qian, Ph.D.

Anne-Marie Falk

ANNE-MARIE FALK, PH.D.
SUPERVISORY EXAMINER